4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 864

[Docket No. FDA-2023-N-4487]

Medical Devices; Hematology and Pathology Devices; Classification of the Container System for the Processing and Storage of Red Blood Cell Components Under Reduced Oxygen Conditions

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is classifying the container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions into class II (special controls). The special controls that apply to the device type are identified in this order and will be part of the codified language for the classification of the container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions. We are taking this action because we have determined that classifying the device into class II (special controls) will provide a reasonable assurance of safety and effectiveness of the device. We believe this action will also enhance patients' access to beneficial innovative devices.

DATES: This order is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The classification was applicable on September 15, 2023.

FOR FURTHER INFORMATION CONTACT: Karen Fikes, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD, 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

Upon request, FDA has classified the container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions as class II (special controls), which we have determined will provide a reasonable assurance of safety and effectiveness. The automatic assignment of class III occurs by operation of law and without any action by FDA, regardless of the level of risk posed by the new device. Any device that was not in commercial distribution before May 28, 1976, is automatically classified as, and remains within, class III and requires premarket approval unless and until FDA takes an action to classify or reclassify the device (see 21 U.S.C. 360c(f)(1)). We refer to these devices as "postamendments devices" because they were not in commercial distribution prior to the date of enactment of the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act).

FDA may take a variety of actions in appropriate circumstances to classify or reclassify a device into class I or II. We may issue an order finding a new device to be substantially equivalent under section 513(i) of the FD&C Act (see 21 U.S.C. 360c(i)) to a predicate device that does not require premarket approval. We determine whether a new device is substantially equivalent to a predicate device by means of the procedures for premarket notification under section 510(k) of the FD&C Act (21 U.S.C. 360(k)) and part 807 (21 CFR part 807).

FDA may also classify a device through "De Novo" classification, a common name for the process authorized under section 513(f)(2) of the FD&C Act; (see also 21 CFR part 860, subpart D). Section 207 of the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) established the first procedure for De Novo classification. Section 607 of the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) modified the De Novo application process by adding a second procedure. A device sponsor may utilize either procedure for De Novo classification.

Under the first procedure, the person submits a 510(k) for a device that has not previously been classified. After receiving an order from FDA classifying the device into class III under

section 513(f)(1) of the FD&C Act, the person then requests a classification under section 513(f)(2).

Under the second procedure, rather than first submitting a 510(k) and then a request for classification, if the person determines that there is no legally marketed device upon which to base a determination of substantial equivalence, that person requests a classification under section 513(f)(2) of the FD&C Act.

Under either procedure for De Novo classification, FDA is required to classify the device by written order within 120 days. The classification will be according to the criteria under section 513(a)(1) of the FD&C Act. Although the device was automatically placed within class III, the De Novo classification is considered to be the initial classification of the device.

When FDA classifies a device into class I or II via the De Novo process, the device can serve as a predicate for future devices of that type, including for 510(k)s (see section 513(f)(2)(B)(i) of the FD&C Act). As a result, other device sponsors do not have to submit a De Novo request or premarket approval application to market a substantially equivalent device (see section 513(i) of the FD&C Act, defining "substantial equivalence"). Instead, sponsors can use the 510(k) process, when necessary, to market their device.

II. De Novo Classification

On January 5, 2022, FDA received Hemanext, Inc.'s request for De Novo classification of the Hemanext One. FDA reviewed the request in order to classify the device under the criteria for classification set forth in section 513(a)(1) of the FD&C Act.

We classify devices into class II if general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but there is sufficient information to establish special controls that, in combination with the general controls, provide reasonable assurance of the safety and effectiveness of the device for its intended use (see 21 U.S.C. 360c(a)(1)(B)). After review of the information submitted in the request, we determined that the device can be classified into class II with the establishment of special controls. FDA has

determined that these special controls, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of the device.

Therefore, on September 15, 2023, FDA issued an order to the requester classifying the device into class II. In this final order, FDA is codifying the classification of the device by adding 21 CFR 864.9115.[1] We have named the generic type of device container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions, identified as a device intended for medical purposes that is used to process and store Red Blood Cell components and reduce oxygen levels in the storage environment.

FDA has identified the following risks to health associated specifically with this type of device and the measures required to mitigate these risks in table 1.

Table 1.--Container System for the Processing and Storage of Red Blood Cell Components Under Reduced Oxygen Conditions Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Toxicity that can result from contact of the component materials of the device with the red blood cells or patient's body	Biocompatibility evaluation
Toxicity of leached materials, or residual chemical sterilant, when in contact with red blood cells or transfused to patient	Extractables and leachables testing
Infection	Sterilization validation; Endotoxin testing; and Container closure evaluation
Transfusion of poor quality red blood cells because of inadequate storage conditions or device malfunction	Nonclinical and clinical studies; Shelf-life testing; and Performance testing
Blood exposure because of device malfunction	Performance testing
Transfusion of poor quality red blood cells due to processing of Red Blood Cells components collected from donors with hemoglobin S	Labeling

FDA has determined that special controls, in combination with the general controls, address these risks to health and provide reasonable assurance of safety and effectiveness. For a

[1] FDA notes that the "ACTION" caption for this final order is styled as "Final amendment; final order," rather than "Final order." Beginning in December 2019, this editorial change was made to indicate that the document "amends" the Code of Federal Regulations. The change was made in accordance with the Office of Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

device to fall within this classification, and thus avoid automatic classification in class III, it would have to comply with the special controls named in this final order. The necessary special controls appear in the regulation codified by this order. This device is subject to premarket notification requirements under section 510(k) of the FD&C Act. At the time of classification, container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions is for prescription use only. Prescription devices are exempt from the requirement for adequate directions for use for the layperson under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) and 21 CFR 801.5, as long as the conditions of 21 CFR 801.109 are met.

III. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IV. Paperwork Reduction Act of 1995

This final order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 860, subpart D, regarding De Novo classification have been approved under OMB control number 0910-0844; the collections of information in 21 CFR part 814, subparts A through E, regarding premarket approval, have been approved under OMB control number 0910-0231; the collections of information in part 807, subpart E, regarding premarket notification submissions, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 820, regarding quality system regulation, have been approved under OMB control number 0910-0073; and the collections of information in 21 CFR part 801, regarding labeling, have been approved under OMB control number 0910-0485.

List of Subjects in 21 CFR Part 864

Blood, Medical devices, Packaging and containers.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 864 is amended as follows:

PART 864--HEMATOLOGY AND PATHOLOGY DEVICES

1. The authority citation for part 864 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

2. Add § 864.9115 to subpart J to read as follows:

§ 864.9115 Container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions.

(a) *Identification*. A container system for the processing and storage of Red Blood Cell components under reduced oxygen conditions is a device intended for medical purposes that is used to process and store Red Blood Cell components and reduce oxygen levels in the storage environment.

(b) *Classification*. Class II (special controls). The special controls for this device are:

(1) The intended use of the device must specify:

(i) The Red Blood Cell components that can be processed and stored including acceptable anticoagulants and additive solutions;

(ii) The hold time after Red Blood Cell component collection;

(iii) The processing capacity (volume) of the device; and

(iv) The storage temperature and dating period of processed Red Blood Cell components.

(2) Studies must demonstrate that the device is biocompatible and include detailed documentation of the biocompatibility evaluation.

(3) Performance testing and nonclinical studies must include a detailed study of leached materials extracted under conditions similar to clinical usage of the device, and a toxicologic risk assessment of those extracted or leached materials.

(4) Performance testing must support sterility of the device and include sterilization validation, endotoxin testing, and container closure integrity evaluation.

(5) Nonclinical and clinical studies must include evaluation of red blood cell quality throughout the duration of storage based on in vitro and in vivo studies, including hemolysis and red blood cell survival and recovery.

(6) Performance studies must include:

(i) Detailed documentation of functional and mechanical testing, including evaluation of oxygen and, if applicable, carbon dioxide levels during Red Blood Cell components storage; and

(ii) Detailed documentation of device shelf-life testing demonstrating continued sterility, package integrity, and functionality over the identified shelf life.

(7) The labeling must include a contraindication against processing Red Blood Cell components collected from donors with hemoglobin S.

Dated: November 3, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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